

## **REMARKS**

Claims 1, 19, 20, 26, and 27 remain in the application. Claims 1, 19, 20, 26, and 27 have been amended. Reconsideration of this application, as amended, is respectfully requested.

Claim 1 has been amended to address the rejections based on 35 U. S. C. § 112. Support for these amendments can be found as follows:

Change	Support in the specification (paragraph)
"Protein" to "First Macromolecule"	0052; 0056
"Solid-surface" to "surface"	0049; 0056
"Surface-bound protein complex" to "complex comprising the First Macromolecule bound to the reactive surface"	0050; 0051
"Solid surface:protein:Second Macromolecule stable complex" to "stable complex comprising the reactive surface, the First Macromolecule, and the at least one Second Macromolecule"	0056; 0060

Claim 1 has been further amended to specify that the stable complex formed in step d) comprises the reactive surface, the First Macromolecule, and the at least one Second Macromolecule and that a covalent bond exists between the First Macromolecule and the at least one Second Macromolecule. Support for these amendments can be found at paragraphs 0037, 0056, and 0060 of the specification.

Claim 19 has been amended to specify that the First Macromolecule is a single antibody. Support for this amendment can be found at paragraph 0059 of the specification.

Claim 20 has been amended to specify that the conjugate comprises a plurality of Second Macromolecules, which can be the same or different, and that the Second Macromolecules are antibodies. Support for this amendment can be found at paragraph 0060 of the specification.

Claim 26 has been amended to delete the phrase "preferably the first" and the term "final." Claim 26 has been further amended to change "other macromolecules" to "other macromolecule or macromolecules."

Claim 27 has been amended to change "the macromolecule" to "one of the macromolecules."

Claims 26 and 27 conform to claim 1.

Claims 1, 19, 20, 26, and 27 were rejected under 35 U. S. C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. This rejection has been addressed by the rewriting of claims 1, 19, 20, 26, and 27.

Claim 1 was rejected under 35 U. S. C. §102(e) as being anticipated by Yu et al. (U. S. 6,492,105). This rejection is respectfully traversed for the following reasons.

Yu et al., U. S. Patent No. 6,492,105 (hereinafter "Yu et al."), discloses polypeptide binding molecules prepared using solid phase peptide synthesis. Solid-phase synthesis begins at the carboxy-terminus of the putative polypeptide by coupling a protected amino acid to a suitable resin, which reacts with the carboxy group of the C-terminal amino acid to form a bond that is readily cleaved later, such as a halomethyl resin, hydroxymethyl resin, aminomethyl resin, benzhydrylamine resin, or t-alkyloxycarbonyl-hydrazide resin. After removal of the  $\alpha$ -amino protecting group with, for example, trifluoroacetic acid in methylene chloride and neutralizing in, for example, TEA, the next cycle in synthesis is ready to proceed. The remaining  $\alpha$ -amino and, if necessary, side-chain-protected amino acids are then coupled sequentially in the desired order by condensation to obtain an intermediate compound connected to the resin. After the desired amino acid sequence has been completed, the intermediate polypeptide is removed from the resin support by treatment with a reagent, such as liquid HF and one or more thio-containing scavengers, which not only cleaves the polypeptide from the resin, but also cleaves all the remaining side-chain protecting groups. Following HF cleavage, the protein sequence is washed with ether, transferred to a large volume of dilute acetic acid, and stirred at pH adjusted to about 8.0 with ammonium hydroxide. Upon pH adjustment, the polypeptide takes its desired conformational arrangement.

Yu et al. describes a cleavable bond for forming high affinity binding molecules to isolate desired components of a biological fluid, and then to release these desired components after washing off undesired components. In Yu et al., there is no covalent bond between the First Macromolecule analogue (an antibody) and the Second Macromolecule analogue (the component to be isolated). For this reason, it is submitted that Yu et al. does not anticipate claim 1.

Claims 19 and 20 were rejected under 35 U. S. C. §103(a) as being unpatentable over Yu et al. (U. S. 6,492,105). This rejection is respectfully traversed for the following reasons.

Claims 19 and 20 depend from claim 1. For the same reasons that Yu et al. does not anticipate claim 1, Yu et al. does not render claims 19 and 20 obvious to one of ordinary skill in the art.

Claims 1, 19, and 20 were rejected under 35 U. S. C. §102(e) as being anticipated by Schwartz (U. S. 2003/0013857 A1). This rejection is respectfully traversed for the following reasons.

Schwartz, U.S. Patent Application Publication 2003/0013857 A1 (hereinafter "Schwartz"), discloses modified solid supports that include solid supports that have been modified by reaction with a bifunctional reagent that possess a hydrazine or oxyamino group. These modified solid supports are useful in immobilization of biomolecules that possess or are modified to possess a carbonyl group. In one embodiment, aliphatic bifunctional hydrazide reagents are provided. These reagents include a cleavable bond for further manipulation. Cleavable bonds include, but are not limited to, acid cleavable, photocleavable and disulfide bonds.

Schwartz does not disclose the reaction of a first macromolecule bound to a surface with a second macromolecule to prepare a conjugate on the surface. Schwartz does not disclose linking of a first macromolecule to a surface, then modifying the first macromolecule by linking another macromolecule to it, and then releasing the modified first macromolecule from the surface. For these reasons, Schwartz does not anticipate claim 1. Claims 19 and 20 depend from claims 1. For the same reasons that Schwartz does not anticipate claim 1, Schwartz does not anticipate claims 19 and 20.

Claim 1 was rejected under 35 U. S. C. §103(a) as being unpatentable over Merrifield (Reference AK of PTO form 1449). This rejection is respectfully traversed for the following reasons.

Merrifield, Solid Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide, Journal of American Chemical Society, USA, 85, pp. 2149-2154 (July 1963) (hereinafter "Merrifield"), discloses the stepwise addition of protected amino acids to a growing peptide chain which was bound by a covalent bond to a solid resin particle. This provided a procedure whereby reagents and by-products were removed by filtration, and the recrystallization of intermediates was eliminated.

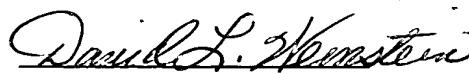
Merrifield describes solid phase synthesis of peptides, not macromolecules, through the use of conditions suitable for organic chemical synthesis. Merrifield attaches a first amino acid to a second amino acid, the second amino acid to a third amino acid, and so forth until a peptide is formed on the solid phase. In the present invention, a first macromolecule is attached to a second macromolecule, and so forth until a chain of macromolecules is formed. Because individual amino acids are not macromolecules, it is submitted that Merrifield does not render claim 1 obvious to one of ordinary skill in the art.

In view of the foregoing, it is submitted that claims 1, 19, 20, 26, and 27, as amended, are in condition for allowance, and official Notice of Allowance is respectfully requested.

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Abbott Laboratories  
D-377 AP6A-1  
100 Abbott Park Road  
Abbott Park, Illinois 60064-3500  
Telephone: (847) 937-6182

Respectfully submitted,  
John C. Russell

  
David L. Weinstein  
Registration No. 28, 128  
Attorney for Applicants